Clinical and Epidemiologic Research

Treating Amblyopia with Liquid Crystal Glasses: A Pilot Study

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PURPOSE. To evaluate the use of liquid crystal glasses (LCG) for the treatment of amblyopia caused by refractive errors, strabismus, or both.

METHODS. In this noncomparative, prospective, interventional case series, 28 children (age range, 4–7.8 years) with monocular amblyopia participated, of which 24 completed the study. In the LCG, the occluding and nonoccluding phases of the flicker were electronically set in all patients at a fixed rate. The rate was set so that accumulated occlusion was 5 hours during 8 hours of wear time. Occlusion was applied only to the good eye. All 24 children were followed up regularly for 9 months. Best corrected VA for distance and near, fixation patterns, and binocular function were measured. VA for distance was measured with the Snellen chart and for near with the Rossano/Weiss chart.

RESULTS. Mean VA for distance at the end of the study (after 9 months) was 0.59 (SD, 0.16) compared with 0.27 (SD, 0.09) at the beginning (P < 0.001). Most of the children (92%) complied well with the treatment. (Good compliance was defined as wearing the LCG for at least 8 hours per day.) Stereopsis at the end of treatment was good (better than 60 sec arc) in 21% of the children compared with 8% at the beginning. No serious adverse events were recorded.

CONCLUSIONS. The use of LCG in patients with amblyopia yielded an improvement in near and distance VA and in stereopsis. Treatment was well accepted by children and parents. (Invest Ophtalmol Vis Sci. 2010;51:3395–3398) DOI:10.1167/iovs.09-4568

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Clinical and experimental observations have led to the conclusion that an active central nervous system mechanism is responsible for the development of amblyopia. Visual inputs to the cortex are regulated and processed under the control of the dominant eye, which actively suppresses potential inputs from the amblyopic eye.1 Accordingly, for nearly three centuries, the mainstay of treatment for amblyopia has been occlusion of the sound eye. The time advocated for daily patching of the sound eye may vary from a few hours to all of the child's waking hours,2,3 and treatment success rates also vary markedly.4 The wide variation is probably influenced by numerous factors, both known and unknown. Among the known factors that strongly influence visual improvement are poor compliance on the part of parents and the child's unwillingness to occlude the sound eye, the latter factor being especially common at 3 to 7 years of age. It has been suggested that the difficulty in assuring treatment compliance has been overcome by electronic monitoring of patching.5,6 Since patching and atropine treatments are not universally successful and are resisted by some children and parents, there is a need for alternative treatment modalities. As a potential alternative for amblyopia treatment, electronically engineered liquid crystal glasses (LCG) have been devised. The safety and feasibility of this new approach has been reported by our group.7 We extend our previous observations and describe the results of a multicenter pilot study in which this new technology was tested.

Materials and Methods

Liquid Crystal Glasses

The use of LCG, in which an electronic shutter controlled by a preprogrammed microchip is incorporated into the optical refractive lens, represents a new approach to the treatment of amblyopia. The thin glass liquid crystal shutter is applied to the strong eye and is coupled to the refractive lens. The liquid crystal shutter comprises large organic molecules that manifest an electric polarity and are suspended in a gel-like liquid between two thin glass plates coated with thin polarizer film. When an electric voltage is applied to this shutter, the spatial orientation of the suspended molecules is changed and the polarity of the light is rotated. The rotated light is thus blocked by the outer polarizing filter and creates a "black" lens. This action, allows the shutter to alternate between clarity (OFF/OPEN), when no voltage is applied, to a black, highly opaque state, and ON/CLOSED, when voltage is applied.8 (The liquid crystal shutter meets U.S. Food and Drug Administration [FDA] safety standards.) Because of the characteristics of the polarizer film, in the clear state, the lens with the coupled shutter has a slightly greenish color. For balanced viewing, the amblyopic eye lens is slightly tinted, so as to resemble more closely the appearance of the lens with the liquid crystal shutter.

The occlusion process is electronically controlled by a device that comprises a microprocessor with a memory and is powered by rechargeable coin batteries. The rate and duration of each viewing state are preprogrammed at a defined, controlled pace. In clinical practice, the flickering rate can be preprogrammed for individual patients by the
Study Protocol
During enrollment (visit 0) and at each of the six scheduled visits, each patient underwent a thorough eye examination. VA for distance (Snellen chart) and for near (Rossano/Weiss chart) in the sound eye and in the amblyopic eye were assessed while the patient was wearing their prescribed glasses, if any. Scoring of Snellen VA (letters or pictures presented in lines) was according to standard logMAR letters; for example, 20/20 was defined as 1.0, 20/25 as 0.8, and so on. Strabismus was measured for near and distance by the alternate prism cover test. Binocular functions were assessed in cooperative children by using the fly, animals, and circles parts of the Titmus stereopsis test. Slit lamp examination and funduscopy were performed in all patients. Full cycloplegic refraction was performed 40 minutes after tropicamide 0.5% (Mydramide; Fischer Pharmaceutical Labs. Ltd., Tel-Aviv, Israel) and cyclopentolate 1.0% eye drops had been instilled twice with a 15-minute interval between instillations.

Follow-Up
After the baseline visual performances with the LCG had been assessed (visit 1), the parents were briefed about handling and care of the LCG and the need to charge the electronic control batteries overnight. They were also asked to record any unusual events that occurred during the study period and to verify that the electronic shutter was functioning properly when the child started wearing the glasses each morning. They were also taught how to initiate the mechanism manually in case of electronic failure of the shutter’s flicker function and were instructed to inform us of the problem. Each child received two pairs of glasses to ensure continued use in case of a technical problem.

A follow-up visit was scheduled every 5 to 6 weeks during the 9-month period of the study (visits 2-6). After the sixth follow-up visit, wearing of the LCG was discontinued, and corrective regular glasses were prescribed as needed.

During each visit, the parents were asked to subjectively evaluate any technical problems encountered with the LCG, their child’s willingness to wear them, and the length of time for which they were worn. Assessments of visual performance, similar to those performed during visits 0 and 1, were performed in a semisedated fashion. The examiners knew that the patient was participating in the study but did not have clinical information and did not know what each patient’s previous visual performance was.

Data Analysis
The trial data were captured on a computerized CRF (case report form), developed specifically for this study. All subjects who were enrolled in the study and had valid data were included in the analyses (SAS ver. 9.1; SAS Institute, Cary NC). Study data are presented in the form of graphs and tables. Continuous variables are presented as the mean and SD or with a 95% confidence interval. Count data are summarized by a percentage with 95% exact binomial confidence limits where relevant. The statistical significance of the change from baseline VA at each visit was assessed with a Wilcoxon signed ranks test. P < 0.05 or less was considered statistically significant.

RESULTS
Characteristics of the Study Population
Of the 24 children included in the study, 8 were girls and 16 were boys. The age range was 4.0 to 7.8 years, with a mean age of 6.1 (SD, 1.2) years. Amblyopia was present in the right eye in 10 children and in the left eye in 14. Before entering the study, 11 patients had undergone treatment attempts by patching or atropine eye drops, but vision failed to improve in the amblyopic eye. Of those, nine had poor compliance, and two had high compliance but no improvement in vision. Previous offers of treatment by occlusion therapy had been refused by
13 children. The cause of amblyopia was non-alternating esotropia in 6 (25%) children, uncorrected refractive error in 7 (29.2%), and strabismus combined with refractive error in 11 (45.8%).

Visual Performance of the Amblyopic Eye

Figure 1 shows the best corrected VA for distance recorded during the six visits. Mean VA was 0.27 (SD, 0.09) at visit 1 and 0.59 (SD, 0.16) at visit 6.

The steady and consistent improvement of VA during each consecutive visit relative to visit 1 was significant ($P < 0.001$ for each visit). Figure 2 illustrates these performances on a 10-logMar scale.

As shown in Table 1, by visit 6, 79% of the treated children had improved by 3 lines or more or had achieved a VA of 20/30. Notably, 20% had achieved this level of visual performance after the first visit. Improvement in the VA for distance was accompanied by a significant improvement in near vision (reading). More than 80% of the treated patients showed improvement in near VA to 0.4 (normal vision with the Rossano/Weiss chart is 0.5) or better when examined during visit 6.

Binocular Vision

Most of the children in the study had no stereopsis or only gross stereopsis. By the end of the study (visit 6), however, 21% demonstrated good stereopsis (better than 60 sec arc) compared with only 8% at the start of the study.

Visual Functions of the Sound Eye

Distance and near visual acuities of the sound eye remained unchanged throughout the study (data not shown).

Compliance

Of 24 children, 22 (92%) wore the glasses at least 8 hours per day, as requested.

Safety

No serious adverse events were recorded.

The children adjusted to the flickering of the lens of the strong eye easily. Four children had transient headaches, and four events of discomfort were reported. These did not cause them to stop using the LCG. There was no regression (reverse amblyopia) in the VA of the sound eye.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Visit 1</th>
<th>Visit 2</th>
<th>Visit 3</th>
<th>Visit 4</th>
<th>Visit 5</th>
<th>Visit 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved Distance VA, %*</td>
<td>—</td>
<td>21</td>
<td>33</td>
<td>46</td>
<td>54</td>
<td>79</td>
</tr>
<tr>
<td>95% Confidence limits</td>
<td>Lower</td>
<td>13</td>
<td>16</td>
<td>26</td>
<td>33</td>
<td>58</td>
</tr>
<tr>
<td>Upper</td>
<td>—</td>
<td>42</td>
<td>55</td>
<td>67</td>
<td>74</td>
<td>93</td>
</tr>
<tr>
<td>Near VA (%)+</td>
<td>—</td>
<td>38</td>
<td>54</td>
<td>62</td>
<td>79</td>
<td>88</td>
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<tr>
<td>95% Confidence limits</td>
<td>Lower</td>
<td>19</td>
<td>33</td>
<td>41</td>
<td>58</td>
<td>68</td>
</tr>
<tr>
<td>Upper</td>
<td>—</td>
<td>59</td>
<td>74</td>
<td>81</td>
<td>93</td>
<td>97</td>
</tr>
</tbody>
</table>

* Improved distance visual acuity of 3 lines or more or visual acuity of 0.66 (20/30).
+ Near visual acuity of 0.4 or more (Rossano-Weiss chart).

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**Figure 1.** Distance VA of the amblyopic eye at the beginning of the study (visit 1) and during the study.

**Figure 2.** Progress of change from baseline VA, measured as 10 logMAR lines.
DISCUSSION

The results of this study demonstrate an average improvement in VA of 3.5 logMAR lines over 9 months of use of glasses fabricated with liquid crystal technology that provide an electronically controlled, intermittent occlusion of the sound eye, thereby allowing for visual stimuli input to the amblyopic fellow eye. The results also demonstrated that the LCG are safe and have no side effects.

Despite individual variations in the amount of improvement in the tested parameters, at least some improvement in the visual performances of the amblyopic eye was recorded in all treated children. During the first 2 to 5 weeks of the treatment, most of the children were aware of the flickering shutter and the obstruction of visual inputs from the sound eye when the ON stimulus was triggered. However, this awareness decreased over time, and the flickering was hardly noticed. Also of interest is the improvement in binocular visual function observed in some of the children, possibly because the rapid rate of flickering allowed binocular spatial clues to be perceived. The study size of 24 children treated in three different centers did not permit personal tailoring of the treatment period or the flickering rate. It is possible that the success rate for all the tested parameters would be higher if treatment with LCG were individually customized and adapted. This possibility will be examined in a study with a larger number of children, to be performed in the near future.

In the present study, we confirm our previous observations with regard to the safety of the LCG. We also show that amblyopia caused by refractive error, strabismus, or a combination of both can be treated by LCG. Patient compliance with LCG wear in our study was very good. The early withdrawal of four enrolled children occurred for various personal reasons, but all the rest completed the study. Peak improvement in distance VA was achieved very quickly, usually in 20% of the treated children, whereas in most of the group, the maximum improvement was reached only after a longer period. These observations are in line with those reported in studies where the treatment modality was patching. We also found that relative to VA for distance, improvement in reading (near task) acuity was achieved earlier and reached its maximum level earlier. An interesting finding was the significant improvement in stereopsis recorded in 21% of the children. This improvement could have occurred because the use of LCG allows for visual function stimuli of the amblyopic eye while both eyes remain open, enabling binocular interactions to develop. However, one cannot exclude that improved VA in the amblyopic eye resulted in better stereo acuity.

In summary, we demonstrated that LCG is an effective new device for amblyopia treatment. Bearing in mind the need for extended periods of treatment in some types of amblyopia, we are looking into the possibility of programming the pattern of the LCG flickering sequence on an individual basis for those children who need it. We believe that the potential benefit of the treatment could be substantially enhanced if the flickering sequence were adapted to suit the depth of amblyopia, the required duration of treatment, and the age of the patient. Varying the flickering sequence during the treatment period according to the visual function behavior of the amblyopic eye may enhance the LCG’s efficiency.

Many of the amblyopic children wear glasses to correct ametropia. In our study, the glasses were used also for occlusion without the need for additional patch or use of eye drops.

The advantages of the LCG treatment modality demonstrated in the present study could also be further improved by inserting specifically designed electronic processors into the shafts of the glasses. These devices could be programmed to deliver a personally adapted flickering rate, which could also be modulated according to clinical experience and the performance of the amblyopic eye.

References

Liquid Crystal Glasses: Feasibility and Safety of a New Modality for Treating Amblyopia

Amblyopia is the most common cause of monocular visual impairment. Strabismus and anisometropia occurring during childhood are risk factors for amblyopia leading to various levels of poor vision and different responses to currently available treatments.

To overcome the unknown factor of a child's compliance, avoid the blemish of a mechanical patch, and enhance the child's willingness to undergo the antiamblyopic regimen, electronically controlled liquid crystal glasses have been developed. Application of a small electric charge changes the spatial orientation of the suspended crystal molecules within the glasses. Thus, alternation between transmission of light (transparent) or opacification can be achieved at will. A liquid crystal lens in front of the sound eye is used as an intermittent flickering shutter switched between "on," or occlusion (Figure 1), and "off," or light transmission (Figure 2).

For the preliminary evaluation, a pattern of 45 seconds on and 55 seconds off was used. Ten consecutive children (mean ± SD age, 74.3 ± 10.3 months; range, 65-93 months) fulfilling the inclusion criteria for the study were enrolled. During the first enrollment examination (visit 0), a thorough eye examination including cycloplegic refraction was performed. Liquid crystal glasses with the appropriate correction were ordered and the child was invited for reevaluation with the new liquid crystal glasses (visit 1). A follow-up visit was scheduled 5 weeks later (visit 2). Statistical analysis of differences in visual acuity (Snellen decimal score) was performed using a 2-tailed t test. P < .05 was considered statistically significant.

Nine children wore the liquid crystal glasses during all waking hours and were not disturbed in their daily routine. The mean visual acuity for distance after 5 weeks (visit 2) is shown in Table 1. Although some improvement in the visual acuity had been achieved, the differences did not reach statistical significance (P = .22). However, the mean near visual acuity differences (Table 2) reached statistical significance (P = .02). Slitlamp and indirect funduscopy did not show any changes during all of the visits.

This study demonstrates that liquid crystal technology can be used for glasses to be able to provide an electronic, controlled, intermittent occlusion of the sound eye allowing for visual stimuli input to the amblyopic fellow eye. We have observed that wearing liquid crystal glasses is safe and does not induce any adverse effects. Liquid crystal glasses achieve the patching effect of a mechanical patch for the sound eye without its cosmetic blemish and without the constant awareness of its presence by the child and his or her environment.

The possibility of manipulating the flickering sequence and adapting it to the depth of amblyopia, the length of needed treatment, and the patient's age while using this device may result in paramount treatment benefits.
Table 2. Visual Acuity for Near During Visits 0 and 2

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Visit 0</th>
<th>Visit 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>2</td>
<td>0.3</td>
<td>0.5</td>
</tr>
<tr>
<td>3</td>
<td>0.3</td>
<td>0.5</td>
</tr>
<tr>
<td>4</td>
<td>0.2</td>
<td>0.5</td>
</tr>
<tr>
<td>5</td>
<td>0.4</td>
<td>0.5</td>
</tr>
<tr>
<td>6</td>
<td>0.2</td>
<td>0.5</td>
</tr>
<tr>
<td>7</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>8</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>9</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>10</td>
<td>0.5</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*Visual acuity for near is expressed as the Snellen decimal score. The mean ± SD visual acuity for near was 0.38 ± 0.13 for visit 0 and 0.50 ± 0.00 for visit 2; P = .02 for the mean visual acuity for near at visit 0 vs visit 2.

To enhance the significance of these preliminary data observations, a larger controlled clinical trial enrolling more patients and following them up for a longer period is needed and is now being planned.

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Financial Disclosure: Dr O. Ben Ezra has financial interest in Ophthalmic Technology Ltd., and is an inventor and developer of the patented association with the use of the liquid crystal glasses technology. Dr Herzog has financial interest in Ophthalmic Technology Ltd., and is a developer of the device based on liquid crystal glasses technology. Dr D. Ben Ezra is a consultant for Ophthalmic Technology Ltd., and has stock shares in the company.


The Eyes, Brain, and Bones of Johann Sebastian Bach

It is true indeed, in this era of specialization, that we tend to look more and more with tunnel vision and sometimes neglect the fact that this is more our own area of expertise. This makes reactions from colleagues in other disciplines most interesting, like the suggestion of Breitenfeld that Bach might have suffered (mild) strokes, at least I in or before 1746 (the year Haussmann depicted Bach on a portrait), and one in July 1750, about 2 weeks for his death.

Since Bach died more than 250 years ago, it seems unlikely the truth will be unravelled anymore. We did try to get closer, though, by proposing a detailed scientific plan to examine the alleged remnants of Bach that are kept in the Thomas Kirche in Leipzig (Germany). Goals were to establish whether it is likely or not that the skeleton belongs to Bach by means of DNA research and to find DNA clues for disease. Unfortunately, this plan recently was rejected by the directorate board of the Thomas Kirche.

Retrospective research on subjects like this is always complicated by limited medical documentation, as is especially the case with Bach. Due to the fact that Bach’s surgeon Taylor left a large written scientific heritage, it is possible to tell something about the operations. Not all left by Taylor is accurate and useful, as he mentions Bach in his 1761 memories, incorrectly stating that Bach was 88 years old, the operation was successful, and Handel was a pupil of Bach.

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